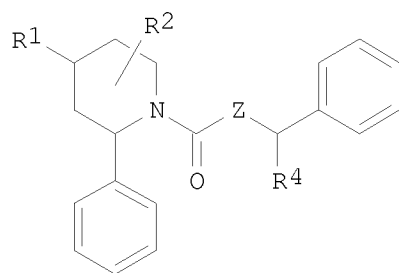
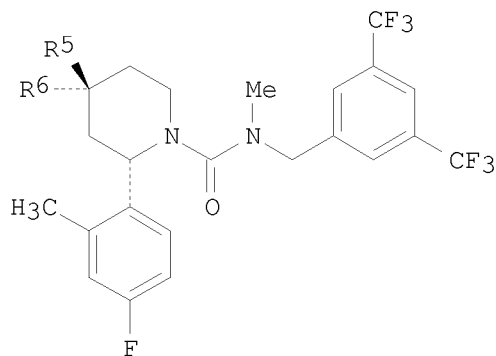


AN 2003:950997 CAPLUS  
 DN 140:16648  
 TI Preparation of N-(arylmethoxycarbonyl)- and N-(arylmethylaminocarbonyl)piperidines as substance P receptor antagonists  
 IN Takahashi, Masami; Miyake, Tsutomu; Moritani, Yasunori; Asai, Hidetoshi; Ishii, Taketoshi; Kono, Rikako  
 PA Tanabe Seiyaku Co., Ltd., Japan  
 SO PCT Int. Appl., 307 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2003099787   | A1   | 20031204 | WO 2003-JP6720  | 20030529 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
|      | JP 2004143139   | A    | 20040520 | JP 2003-148644  | 20030527 |
|      | CA 2487306  | A1   | 20031204 | CA 2003-2487306 | 20030529 |
|      | AU 2003240015   | A1   | 20031212 | AU 2003-240015  | 20030529 |
|      | AU 2003240015   | B2   | 20080103 |                 |          |
|      | BR 2003011410   | A    | 20050315 | BR 2003-11410   | 20030529 |
|      | EP 1513814  | A1   | 20050316 | EP 2003-733139  | 20030529 |
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|      | CN 1656071  | A    | 20050817 | CN 2003-812260  | 20030529 |
|      | NZ 537185   | A    | 20070223 | NZ 2003-537185  | 20030529 |
|      | RU 2294927  | C2   | 20070310 | RU 2004-138594  | 20030529 |
|      | MX 2004PA11764  | A    | 20050331 | MX 2004-PA11764 | 20041126 |
|      | ZA 2004009729   | A    | 20060726 | ZA 2004-9729    | 20041201 |
|      | NO 2004005508   | A    | 20050214 | NO 2004-5508    | 20041216 |
|      | IN 2004CN02950  | A    | 20060217 | IN 2004-CN2950  | 20041227 |
|      | US 2005239829   | A1   | 20051027 | US 2005-515845  | 20050613 |
| PRAI | JP 2002-155744  | A    | 20020529 |                 |          |
|      | US 2002-395342P   | P    | 20020712 |                 |          |
|      | JP 2002-248755  | A    | 20020828 |                 |          |
|      | US 2002-409595P   | P    | 20020911 |                 |          |
|      | WO 2003-JP6720  | W    | 20030529 |                 |          |
| OS   | MARPAT 140:16648  |      |          |                 |          |
| GI   |   |      |          |                 |          |



I



II

AB N-(arylmethoxycarbonyl)- and N-(arylmethylaminocarbonyl)piperidines I [R1 = alkyl, (un)substituted hydroxy, mercapto, carbonyl, sulfinyl, sulfonyl, R11R12N; R2 = H, halogen, (un)substituted hydroxy, amino, alkyl, or carbonyl group; R3, R4 = H, (un)substituted alkyl; R11, R12 = H, (un)substituted carbonyl, sulfonyl, alkyl, heterocyclyl (containing 1-4 nitrogen, oxygen, or sulfur atoms); R11R12N may form an (un)substituted heterocyclyl moiety from the list of piperidinyl, hexahydroazepinyl, pyrrolidinyl, imidazolidinyl, hexahydropyrimidinyl, thiazolidinyl, morpholinyl, triazolyl, tetrazolyl, purinyl; Z = O, NR3; both of the explicit Ph rings may be substituted] such as II are prepared as tachykinin receptor antagonists (and particularly substance P receptor antagonists) for the treatment of inflammation, allergies, pain, nausea, central nervous system and digestive diseases, and urinary and immune disorders. Addition of 4-fluoro-2-methylphenylmagnesium bromide to 4-methoxypyridine followed by acylation with benzyloxycarbonyl chloride, reduction of the dihydropiperidone with zinc and acetic acid, protection of the ketone as the di-Me acetal, reduction of the benzyloxycarbonyl group with hydrogen in the presence of palladium on carbon, addition of 3,5-(F3C)2C6H3CH2NHMe to 1,1'-carbonylimidazole followed by addition of the piperidine, acid cleavage of the acetal, and reduction of the ketone, gives a mixture of the racemic piperidinols II (R5 = H, HO; R6 = HO, H). Approx. 500 example compds. are prepared (no biol. data).

IT 578710-93-7P 578710-95-9P 578710-97-1P  
578711-15-6P 578711-17-8P 578711-24-7P

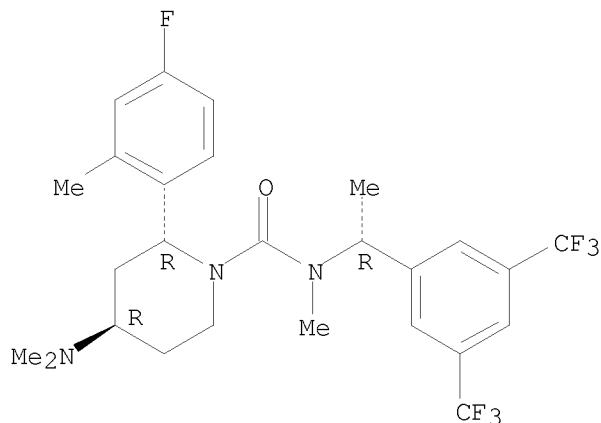
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(title compound; preparation of N-(arylmethoxycarbonyl)- and N-(arylmethylaminocarbonyl)piperidines as substance P receptor antagonists for the treatment of inflammation and conditions such as urinary disorders)

RN 578710-93-7 CAPLUS

CN 1-Piperidinecarboxamide, N-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethyl]-4-(dimethylamino)-2-(4-fluoro-2-methylphenyl)-N-methyl-, monohydrochloride, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

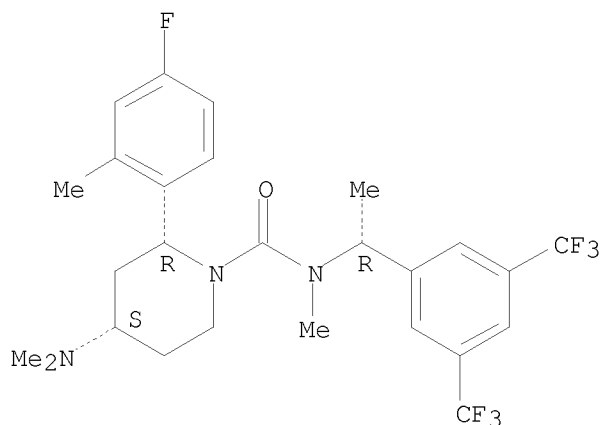


● HCl

RN 578710-95-9 CAPLUS

CN 1-Piperidinecarboxamide, N-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethyl]-4-(dimethylamino)-2-(4-fluoro-2-methylphenyl)-N-methyl-, monohydrochloride, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

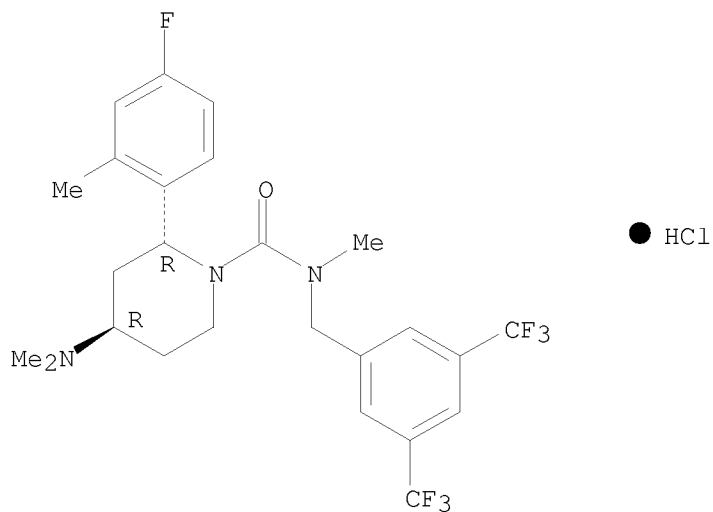


● HCl

RN 578710-97-1 CAPLUS

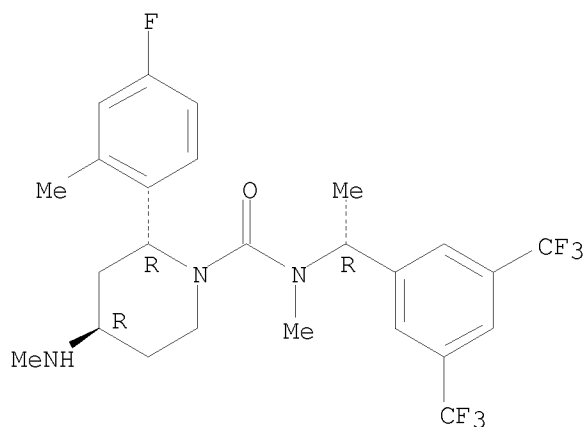
CN 1-Piperidinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-4-(dimethylamino)-2-(4-fluoro-2-methylphenyl)-N-methyl-, monohydrochloride, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



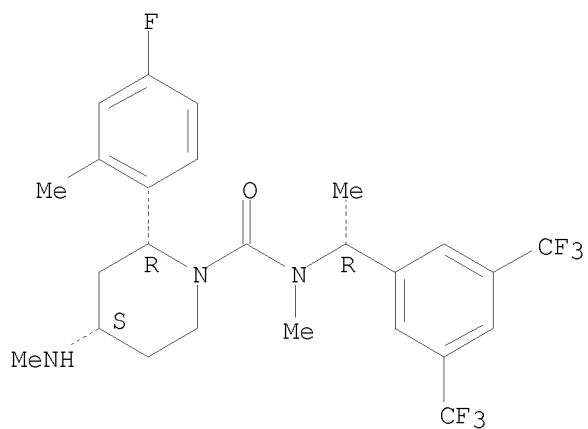
RN 578711-15-6 CAPLUS  
 CN 1-Piperidinecarboxamide, N-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethyl]-  
 2-(4-fluoro-2-methylphenyl)-N-methyl-4-(methylamino)-, monohydrochloride,  
 (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 578711-17-8 CAPLUS  
 CN 1-Piperidinecarboxamide, N-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethyl]-  
 2-(4-fluoro-2-methylphenyl)-N-methyl-4-(methylamino)-, monohydrochloride,  
 (2R,4S)- (9CI) (CA INDEX NAME)

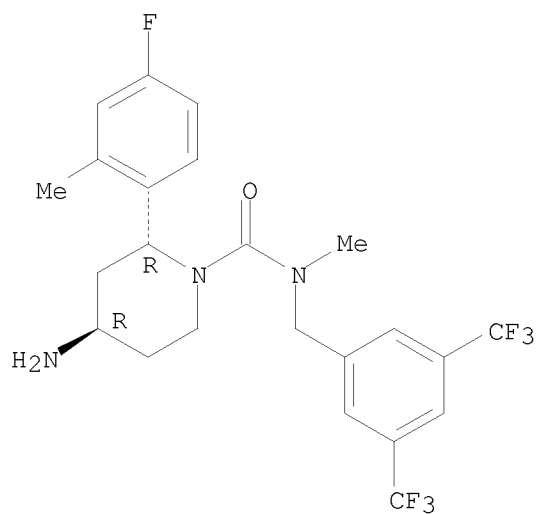
Absolute stereochemistry.



● HCl

RN 578711-24-7 CAPLUS  
 CN 1-Piperidinecarboxamide, 4-amino-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-2-(4-fluoro-2-methylphenyl)-N-methyl-, monohydrochloride, (2R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl